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TITLE: Positioning Bascularized Composite Allotransplantation with the Spectrum of Transplantation

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14. ABSTRACT This proposal utilizes a comprehensive approach to efficiently refine the transplantation of vascularized peripheral tissues (e.g. hand, face) into a useful therapeutic option for individuals in need of advance tissue reconstruction and replacement. The proposal addresses the needs of VCA, namely, a need for therapies that prevent rejection with limited impairment of the recipients protective immunity, and means of accurate monitoring and diagnosis of disorders such as rejection in a manner that will facilitate prompt, specific therapy. Studies include pre-clinical models with proven clinical relevance to assess the performance of clinically applicable therapies. Additionally, we will focus on the establishment of a VCA biorepository and the assessment of clinical material histologically to draw parallels between pre-clinical and clinical studies. We will use our established non-human primate model of VCA with proven clinical relevance to use human reagents so that data derived can be directly applied to the design of clinical protocols.				
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I. Introduction

Recent improvements in body armor have reduced the rate of combat death but increased the rate of soft tissue injury. Vascularized composite allotransplantation (VCA) has recently emerged as a promising strategy for the repair or replacement of lost limbs and complex tissue loss. As VCA is a burgeoning field, there are many fundamental elements relating to its biology and outcome that remain undefined. The entire proposal addresses the need for therapies that prevent rejection with limited impairment of the recipients' protective immunity, and means of accurate monitoring and diagnosis of disorders such as rejection in a manner that will facilitate prompt, specific therapy. The principal objective of this project is to refine vascularized composite allotransplantation (VCA) into a useful therapeutic option for patients in need of advanced tissue reconstruction.

II. Keywords

Biorepository, vascularized composite allograft, nonhuman primates, rejection, belatacept, costimulation blockade, protective immunity, skin, tissue banking.

III. Accomplishments

Site Visit

On November 3, 2014 a site visit from the funding agency was performed. The agenda included various presentations of various resources supporting the Duke Vascularized Composite Allotransplantation Program.

Regulatory Review and Approval Process

The PI transferred from Emory University to Duke University. During this annual report period the award was fully executed on February 11, 2015.

Clinical Research

Following the full execution, the PI initiated the creation of the corresponding study protocols. The PI submitted all key documents for regulatory review for the protocol entitled "Vascularized Composite Allotransplantation Biorepository and Clinical Data Acquisition Protocol" to the Duke University Institutional Review Board (IRB) on June 8, 2015. The PI received institutional approval on September 8, 2015. The required documents were submitted to HRPO on September 28, 2015.

RTR First Investigators Face to Face Consortium Meeting. The first RTR Consortium face to face investigators meeting was held on July 13, 2015 at Duke University (Leading Site). Investigators and research staff from the partnering sites University of Maryland (UM), The Children's Hospital of Philadelphia, and The Hospital of the University of Pennsylvania (CHOP/Penn), and the Louisville VCA Program (Lou) (a collaboration between the Christine M. Kleinert Institute, the Kleinert Kutz Hand Care Center, the Cardiovascular Innovation Institute, the University of Louisville and Jewish Hospital, Part of KentuckyOne Health), attended the meeting. List of attendees below.

Attendees

Rolf Barth, MD (UM)
Stephen Bartlett, MD (UM)
Linda Cendales, MD (Duke)
Jennifer Cheeseman (Duke)
Wayne Hancock, PhD (CHOP/Penn)
Christina Kaufman, PhD (Lou)
Allan D. Kirk, M.D, PhD (Duke)
Frank Leopardi (Duke)
L. Scott Levin, MD (CHOP/Penn)
Mathew Levine, MD (CHOP/Penn)

Michael Marvin, MD (Lou)
Mingqing Song (Duke)
Mehmet Uluer, M.D (UM)
Miranda West, MS (Duke)
Stu Williams, MD (Lou)

The agenda included an update on aims per site and deliverables. The discussion included timelines for regulatory documents between each partnering center and the leading center, SOP's, deliverables per site, and governance was brainstormed. The subsequent meeting/conference call scheduled was decided including the second face to face investigators meeting on July 11, 2016 at Duke University. Additionally, sample and data shipment and future work was laid out for upcoming year. The *VCaci* (VCA Collaborative Initiative) logo was approved unanimously including the use of the logo for consortium related matters and presentations.

Research Accomplishments

- a. IRB submission for the protocol entitled “Vascularized Composite Allograft Biorepository and Clinical Data Acquisition Protocol” received full Duke’s institutional approval on September 8, 2015
- b. The consortium site visit was conducted on July 13, 2015 at Duke University Medical Center. There was representation from each consortium site and each site presenting on their aims as determined by the grant submission.
- c. University of Maryland fully executed their Materials Transfer Agreement with Duke University on July 31, 2015.
- d. Duke Institutional approval was awarded on September 8, 2015
- e. *VCaci* Lab standard operating procedures were sent in a thumb drive to all partnering centers via FedEx on September 20, 2015.
- f. The first investigators conference call was held on September 21, 2015.
- g. Histology digital images from the University of Maryland were uploaded into Aperio the week of October 15, 2015 and a lab conference call was subsequently conducted with the University of Maryland.
- h. All future investigator calls were scheduled until the next face-to-face which is July 11, 2016.
- i. It was decided to continue with the plan to submit an abstract as a *VCaci* to the American Transplant Congress (deadline December 4, 2015).

Pre-Clinical Research

Following full execution of the award on February 11, 2015, the PI initiated the creation of the corresponding study protocols. The PI submitted all key documents for regulatory review for the protocol entitled “Translational Definition of Vascularized Composite Allograft Biorepository and Clinical Data Acquisition Protocol” to the Duke University Institutional Animal Care & Use Committee (IACUC). The PI received IACUC approval of the study on April 23, 2015. The PI submitted the required documents to ACURO and received ACURO approval on June 30, 2015. Subsequently, a portion of the total number of animals were purchased and were received in August 2015. During this report period the animals completed the quarantine period. The first transplant took place after the end of this annual report period.

IV. Impact

The project chosen address needs in VCA including a need for therapies that prevent rejection with limited impairment of the recipient’s protective immunity, and means of accurate monitoring and diagnosis of rejection. In addition, we will also leverage the entire VCA community to develop consensus practice guidelines with regards to diagnosis.

We believe that the results of this Restorative Transplantation Research Cooperative will greatly aid evaluation regarding care of DoD casualties and veterans

V. Changes/Problems

There have been no major changes to the protocol or field of study during this reporting year.

VI. Products

There are no products to report in this annual submission.

VII. Participants & Other Collaborating Organizations

University of Maryland

The Children's Hospital of Philadelphia and The Hospital of the University of Pennsylvania
Louisville VCA Program (Lou) (a collaboration between the Christine M. Kleinert Institute, the Kleinert Kutz Hand Care Center, the Cardiovascular Innovation Institute, the University of Louisville and Jewish Hospital, Part of KentuckyOne Health)

VIII. Special Reporting Requirements

There are no special reporting requirements to acknowledge for this annual reporting period.

IX. Appendices

Not applicable.